

REMARKS

Method-of-use Claims 37-47 are the only claims now pending in this application. Method-of-use Claims 37-47 define a method for prevention of hypertension by use of a renin-inhibiting compound defined in the chemical recitations therein.

\* \* \*

In response to Examiner's request, marked-up versions of the earlier-presented new Abstract and new Page 1 showing a revised "Title" and description of "Related Applications" are attached hereto.

\* \* \*

Applicants' Preliminary Amendment filed 28 November 2001 is objected to under 35 U.S.C. §132 because it purportedly introduces new matter into Applicants' disclosure, namely, as to reference to "prevention" in the new Abstract.

Basis for use of the term "prevention" is found in Applicants' specification as follows:

At Page 17, lines 23-27:

"The phrase 'hypertensive subject' means, in this context, a subject suffering from or afflicted with the effects of hypertension or susceptible to a hypertensive condition if not treated to prevent or control such hypertension."

At Page 72, lines 11-14:

"Therapeutically effective doses of the compounds of the present invention required to prevent or arrest the progress of the medical condition are readily ascertained by one of ordinary skill in the art."

Clearly, there is basis for term "prevention" as found in foregoing citations from Applicants' originally-filed specification. Accordingly, the objection under 35 U.S.C. §1.32 is overcome.

\* \* \*

Method-of-use Claims 37-47 stand rejected under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over:

Claims 23-33 of U.S. Patent No. 5,223,535

and

Claims 1-11 of U.S. Patent No. 6,342,642.

Each of the foregoing cited U.S. Patents is co-owned, with the subject Application, by Applicants' Assignee.

This rejection is rendered moot by introduction herewith of Terminal Disclaimers for the claims of the subject Application over the terms of each of said cited U.S. Patent.

\* \* \*

Claims 37-47 stand rejected under 35 U.S.C. §112, first paragraph, on the ground that the claimed embodiment of "prevention" lacks description and enablement in the originally-filed specification.

Attention is directed to Applicants' citations, above, as to two portions of Applicants' Specification which provide basis, support and teaching for use of the term "prevention".

Moreover, description and enablement of the claimed methods of prevention for the disorders described in Applicants' specification are found at:

Page 17, lines 8-30, where both prevention and treatment of circulatory disorders are described.

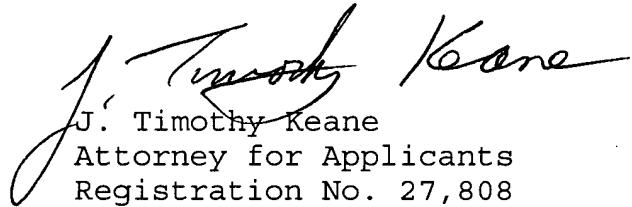
Page 72, line 1, through Page 74, line 14, where various compositions and methods incorporating Renin Inhibitors recited in Method-of-Use Claims 37-47, are described for prevention and treatment along with methods of administration orally and by injection, along with doses and suitable adjuvants.

For these reasons, rejection of Claims 37-47 under 35 U.S.C. §112, first paragraph, should be withdrawn.

\* \* \*

In view of foregoing Remarks, Claims 37-47 should be in condition for allowance.

Respectfully submitted,



J. Timothy Keane  
Attorney for Applicants  
Registration No. 27,808  
314-274-9090

Pharmacia Corporation  
Global Patent Department  
P.O. Box 1027  
Chesterfield, MO 63006

Attachments

Marked-Up Versions of New Abstract and Amended Page 1  
Clean Copies of New Abstract and Amended Page 1

USE OF PROPARGYL GLYCINE AMINO PROPARGYL DIOL  
COMPOUNDS FOR [TREATMENT] PREVENTION OF HYPERTENSION

RELATED APPLICATIONS

5        [This application is a continuation-in-part of Application Serial No. 07/784,272, filed on 29 October 1991.] This application is a divisional of U.S. Application Serial No. 09/479,280, filed 6 January 2000, which issued as U.S. Patent No. 6,342,624, which is a  
10 continuation of Application Serial No. 09/969,522 filed on 13 November 1997, which is a continuation of Application Serial No. 08/771,334, filed on 16 January 1996, which is a continuation of Application Serial No. 08/199,237, filed 28 February 1994, which issued 16 January 1996 as U.S. Patent 5,484,812, which is a  
15 continuation-in-part of Application Serial No. 07/784,272, filed on 29 October 1991, which issued on 29 June 1993 as U.S. Patent 5,223,535.

FIELD OF THE INVENTION

20        Renin-inhibiting compounds are known for control of hypertension. Of particular interest herein are compounds useful as renin inhibiting agents.

BACKGROUND OF THE INVENTION

25        Renin is a proteolytic enzyme produced and secreted into the bloodstream by the juxtaglomerular cells of the kidney. In the bloodstream, renin cleaves a peptide bond in the serum protein angiotensinogen to produce a decapeptide known as angiotensin I. A second enzyme known as angiotensin converting enzyme, cleaves angiotensin I to produce the octapeptide known as angiotensin II. Angiotensin II is a potent pressor agent responsible for vasoconstriction and elevation of cardiovascular pressure. Attempts have been made to control hypertension by blocking the action of renin or by blocking the formation of angiotensin II in the body with inhibitors of angiotensin I converting enzyme.

35        Classes of compounds published as inhibitors of the action of renin on angiotensinogen include renin antibodies, pepstatin and its analogs, phospholipids, angiotensinogen analogs, pro-renin related analogs and peptide aldehydes.

**USE OF PROPARGYL GLYCINE AMINO PROPARGYL DIOL COMPOUNDS**  
**FOR [TREATMENT] PREVENTION OF HYPERTENSION**

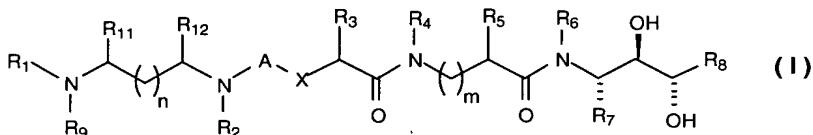
**ABSTRACT**

5

Compounds characterized generally as propargyl glycine amino propargyl diol derivatives are useful for [treatment] prevention of hypertension.

Compounds of particular interest are those of Formula I

10



wherein A is selected from CO and SO<sub>2</sub> wherein X is selected from oxygen atom and methylene; wherein each of R<sub>1</sub> and R<sub>9</sub> is a group independently selected from hydrido, methyl, ethyl, n-propyl, isopropyl, benzyl, b, b, b-trifluoroethyl, t-butyloxycarbonyl and methoxymethylcarbonyl, and wherein the nitrogen atom to which R<sub>1</sub> and R<sub>9</sub> are attached may be combined with oxygen to form an N-oxide; wherein R<sub>2</sub> is selected from hydrido, methyl, ethyl and isopropyl; wherein R<sub>3</sub> is selected from benzyl, cyclohexylmethyl, phenethyl, imidazolemethyl, pyridylmethyl and 2-pyridylethyl; wherein each of R<sub>5</sub> and R<sub>8</sub> is independently propargyl or a propargyl-containing moiety; wherein R<sub>7</sub> is cyclohexylmethyl; wherein each of R<sub>4</sub> and R<sub>6</sub> is independently selected from hydrido and methyl; wherein each of R<sub>11</sub> and R<sub>12</sub> is independently selected from hydrido, alkyl and phenyl; wherein m is zero; and wherein n is a number selected from zero through three; or a pharmaceutically-acceptable salt thereof.